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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/328,296 06/08/99 SIEGALL

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HM12/0830

EXAMINER

CANELLA, K

ART UNIT

PAPER NUMBER

1642

DATE MAILED:

08/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/328,296

Applicant(s)

Slegall et al

Examiner

Karen Canella

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 months MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 21-25, 34-36, and 38-68 is/are pending in the application.
- 4a) Of the above, claim(s) 35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 21-25, 34, 36, and 38-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 12
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

Art Unit: 1642

Response to Amendment

1. Claims 1, 2, 8, 9, 21-24 and 36 have been amended. Claims 10-20, 26-33 and 37 have been amended. Claims 38-68 have been added. Claims 1-9, 21-25, 34-36 and 38-68 are pending. Claim 35, drawn to a non-elected invention, remains withdrawn from consideration. Claims 1-9, 21-25, 34, 36 and 38-68 are under consideration.

Claim Rejections Maintained

2. The rejection of claims 9, 21-25 and 36 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the monoclonal antibody S2C6 and fragments thereof, does not reasonably provide enablement for a protein comprising one or more substitutions or insertions in the primary amino acid sequence relative to that of the monoclonal antibody S2C6, or a protein variant of S2C6. The rejection of claims 1, 3, 7, 8 and 38-68 are also made for the same reasons of record. The specification teaches that the monoclonal antibody S2C6 binds to the CD40 receptor on B-cells. The specification teaches that this antibody is anti-neoplastic and augments the interaction of CD40 receptor with the CD40 ligand. It is well known in the art that activation of the CD40 receptor on a B-cell with the CD40 ligand cause growth and expansion of said B-cell. Although one of skill in the art could find antibodies which vary in amino acid sequence from S2C6 that cause an enhancement of the binding of CD40 to the CD40 receptor, one of skill in the art would not know if said antibody also had anti-neoplastic effects as the specification does not give any guidance toward the activation of the CD40 receptor and any antineoplastic effects on B-cells. Bjorck et al (immunology, 1996, Vol. 87, pp. 291-295) teaches that antibodies which bind to CD40 can induce B-cell differentiation, in opposition to B-cell proliferation. However, the instant specification does not teach binding at a specific epitope, or the generation of a signal produced by binding of a variant of S2C6 antibody which would induce apoptosis or terminal differentiation in B-cells. Given this lack of guidance on the mechanism by

Art Unit: 1642

which the S2C6 antibody induces an antineoplastic effect, one of skill in the art would not know how to make variants of S2C6 that exerted the same effect.

3. The rejection of claims 1, 2, 3, 7, 8, and 34 under 35 U.S.C. 102(b) as being anticipated by either Kwekkeboom et al (Immunology, 1993, Vol. 79, pp. 439-444), is maintained for reasons of record.

4. The rejection of claims 1, 2, 3, 7, 8, and 34 under 35 U.S.C. 102(e) as being anticipated by de Boer (USP 5,874,082), is maintained for reasons of record. ✓

5. The rejection of claims 1, 2, 3, 7, 8, 34, and 4 under 35 U.S.C. 103(a) as being unpatentable over Kwekkeboom et al in light of Uckun et al (Blood, 1990, Vol. 76, pp. 2449-2456), is maintained for reasons of record.

6. The rejection of claims , 2, 3, 7, 8, 34, 4 and 5 under 35 U.S.C. 103(a) as being unpatentable over Kwekkeboom et al and Uckun as applied to claims 2, 3, 7, 8, 34, and 4 above, and further in view of Siegall, is maintained for reasons of record.

7. The rejection of claims 1, 2, 3, 7, 8, 34 and 6 under 35 U.S.C. 103(a) as being unpatentable over de Boer (USP 5,874,082) in light of what is suggested in de Boer (USP 5,874,082), is maintained for reasons of record.

8. The rejection of claims 1, 2, 3, 7, 8, and 34 under 35 U.S.C. 102(b) as being anticipated by or Bjorck et al (Immunology, 1994, Vol. 83, pp. 430-437), is withdrawn. Applicant has argued that the antibodies disclosed by Bjorck inhibit the binding of CD40 ligand to CD40 immobilized receptor to a greater extent than S2C6, therefore said antibodies could not increase the binding of CD40 ligand to CD40 receptor.

9. Applicant argues that none of the antibodies disclosed by Kwekkeboom et al) or Boer (USP 5,874,082) disclose an antibody with the same function and activity as S2C6. This has been considered but not found persuasive as the rejected claims do not specify that the variant of S2C6 have the same functions and activities as S2C6 beyond that of increasing the binding of CD40

Art Unit: 1642

ligand. Applicant provided no arguments as to the increase or decrease of binding of the CD40 ligand in the presence of these antibodies.

New Claim Rejections

10. Claims 1-9, 21-25, 34, 36 and 38-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirano et al in view of Bjork et al (immunology, 1994 Vol. 83, pp. 430-437). Hirano et al teach the inhibition of human breast carcinoma cells expressing the CD40 receptor by a soluble CD40 ligand. Hirano et al do not teach the inhibition of said carcinoma cells by an antibody which increases the binding of CD40 ligand to the CD40 receptor. Bjork et al teach that the antibody S2C6 positively cooperates in the binding of CD40 ligand to CD40 receptor. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the S2C6 antibody with CD40 ligand to inhibit the growth of human carcinoma cells. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Hirano et al on the CD40 ligand inhibition of human carcinoma cells expressing the CD40 receptor and the teachings of Bjoreck et al on the positively cooperation between the S2C6 antibody and the binding of CD40 ligand. One of skill in the art would have concluded that if binding of CD40 ligand was inhibitory in the case of human carcinoma cells, enhanced binding of CD40 ligand would increase the inhibition.

11. Claim 1, 6, 8, 9, 21, 22, 23, 24, 44, and 45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1, 6, 8, 9, 21, 22, 23, 24, 44, and 45 are drawn to hybridoma deposited with the ATCC and assigned the accession number PTA-110. Applicant's referral to this deposit of PTA-110 on page 58 of the specification is insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposit was made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by

Art Unit: 1642

applicant, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when a deposit is made under the provision of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State.

12. All other rejections and objections as stated in Paper No. 9 are withdrawn.


Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

August 27, 2001


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